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POLYPHARMACY AND THE POTENTIAL OCCURRENCE OF DRUG – DRUG INTERACTIONS (DDIS) AMONG GERIATRIC OUTPATIENTS

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ABSTRACT
Number of elderly across the world is increasing over the year. Among the elderly, physical and biological changes along with increasing number of diseases contribute to multiple medications. Polypharmacy in geriatric patients increases the risk of adverse drug reactions (ADRs) and drug-drug interactions (DDIs). Objective: This study aims to evaluate polypharmacy and potential DDIs occurrence among geriatric outpatients. A Retrospective observational study was conducted in Geriatric Outpatient Clinic at Wangaya Regional General Hospital. Data was collected using medical records from May – June 2025. DDIs were identified and classified using Lexicomp Drug Interactions database. Data distribution and statistical analyzes were performed using Spearman correlation test. Statistical hypothesis tests with p-value less than 0.05 were considered statistically significant. This study involves 167 patients. Majority of the patients (47.3%) are in the young elderly group. Among the patients, 50.3% was considered as minor polypharmacy, 44.9% as major polypharmacy, and 1.2% as excessive polypharmacy. Most of DDIs type found in our study was Type C DDIs (45.9%) followed by Type B (31.9%). We found a statistically significant association between number of comorbidities, polypharmacy and DDIs. High prevalence and significant correlation were found between polypharmacy and potential occurrence of DDIs were found among geriatric outpatients. The finding of this study indicates the need for further research to develop strategies that can reduce the occurrence of polypharmacy and DDIs.

Keywords: DDIs; elderly, geriatric; polypharmacy

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INTRODUCTION

The number of elderly in Indonesia has increased significantly, from 18 million (7.6%) in 2010 to 27 million (10%) in 2020 (Awali et al., 2024). Elderly is defined as an individual who is 60 years or above (Febriyanti et al., 2023). Most elderly experience aging process accompanied with various physiological and biological changes that affect the body and quality of life. These conditions, along with increasing chronical disease as the age advanced, leads to greater number of medications being required (Awali et al., 2024).

The concurrent use of multiple medications at the same time in one individual is known as Polypharmacy, which is often necessary to manage multiple chronic conditions that increase with age. However, as the number of medications increase, the risk of adverse drug reactions (ADRs) and drug-drug interactions (DDIs) also increase (Alhumaidi et al., 2023). Polypharmacy is defined by World Health Organization (WHO) as the use of three or more medications. It is considered as minor polypharmacy when using 2-4 drugs, major polypharmacy when using 5 or more drugs, and excessive polypharmacy when using 10 or more drugs (Lozano-Lozano et al., 2024). As the number of medications increase, the risk of adverse drug reactions are also higher. The likelihood of ADRs is 13% when taking 2 drugs, increases to 58% with 5 drugs, and reaches 82% with 7 or more drugs (Alhumaidi et al., 2023).

According to WHO in 2015, the global prevalence of polypharmacy ranges from 38% to 91% (Febriyanti et al., 2023). Studies across European countries and Israel in 2024 showed that the prevalence of polypharmacy among patients over 64 years old ranged from 26% to 40% (Nicholson et al., 2024). In 2015, a study on outpatients in Haji Adam Malik General Hospital in Medan, Indonesia found 78% DDIs in elderly patients with metabolic disease (Khairani et al., 2024). Another study conducted at a hospital in Surabaya in 2023 showed the prevalence of polypharmacy among geriatric patients discharge from inpatient care was 52.15% (Faisal et al., 2024).

The concurrent use of multiple medications can lead to DDIs, a condition in which the activity of one drug affects the others, this could be synergistic, antagonistic, or could create a new effect (Vegada et al., 2020). Other factors that could affect the risk of medication in elderly include exposure to multiple prescriptions from different doctors, depression, insomnia, cognitive and functional impairment, such as urinary incontinence and sarcopenia. In some cases, uncoordinated prescribing could increase the risk of DDIs, potentially leading to harmful drug reactions (Yan et al., 2025). Based on the above considerations, the aim of this study is to evaluate the occurrence of polypharmacy and DDIs among elderly patients attending the Geriatric Outpatient Clinic at Wangaya Regional General Hospital, as well as to analyze the correlation between the two.

METHOD

This study is an observational study with retrospective approach, conducted using medical record data in Geriatric Outpatient Clinic at Wangaya Regional General Hospital. This study was carried out following ethical approval from the Health Research Ethics Committee of Wangaya Regional General Hospital (No.000.9.2/6018/RSUDW). Data sources included all records that met the inclusion and exclusion criteria from May – June 2025

The inclusion criteria are patients aged ≥ 60 years with complete medical records. The exclusion criteria are patients who visited the clinic only for pre-procedural assessment, those who were hospitalized from the polyclinic, and the data from patients who had monthly follow up visits with the same medications was only taken once. Drug interactions were assessed using the Lexicomp Drug Interactions database, which categorizes potential interactions based on their clinical significance. In this system, categories range from A to X, where type A represents no known interaction, progressing through types B, C, and D to type X, which denotes combinations that should be strictly avoided. This classification allows for systematic evaluation of drug safety and the need for clinical intervention. The analyzed variables were age, which consists of young elderly (60-69 years), middle elderly (70-79 years), and old elderly (≥ 80 years), sex, number of comorbidities, polypharmacy which consists of minor (2-4 drugs), major (≥ 5 drugs), and excessive (≥ 10 drugs), and number of identified DDIs. Univariate dan bivariate analyses were performed on these data. The pearson or spearman correlation test was applied to assess the relationships between age, number of medications, and number of drug interactions. A p-value of <0.05 was considered statistically significant.

RESULT

The data were obtained from 167 patients aged over 60 years who were being treated at our geriatric polyclinic. Patients' mean age was 70.36 ± 6.4 years ranging from 60 to 90 years (Table 1). Majority of the patients belonged to the Young Elderly (47.3%). The number of female patients were slightly more than male patients, accounting for 50.3% and 49.7%, respectively (Table 1). The most comorbidity that the patients have is Hypertension (73,6%) followed by Diabetes Mellitus (54,4%) and Hyperlipidaemia (23,9%). (Table 1). The average number of drugs consumed by the patients was 4.63 ± 2.0 ranging from 1 to 11 drugs. (Table 2) Majority of the patients have minor polypharmacy (50.3%), and 1,2% of the patients have excessive polypharmacy. The most commonly used drugs in population is Kandesartan (48.5%) followed by Vitamin B Kompleks (41.3%), Amlodipin (29.9%), Asam Folat (25.7%), and Long Acting Insulin (23.9%). (Table 2)

Table 1.
Demographics and Comorbidities

Variable	**f** (%)
Age	Mean 70.36 ± 6.4
Young Elderly (60-69 years)	79 (47.3%)
Middle Elderly (70-79 years)	72 (43.1%)
Old Elderly (≥ 80 years)	16 (9.6%)
Sex	
Male	83 (49.7%)
Female	84 (50.3%)
Comorbidity	
Hypertension	123 (73.6%)
Diabetes Mellitus	91 (54.4%)
Hyperlipidaemia	40 (23.9%)
Hyperuricaemia	17 (10.2%)
Neuropathy	17 (10.2%)
Dyspepsia	15 (8.9%)

Table 2.
Polypharmacy and most commonly used drugs

Variable	**f** (%)
Polypharmacy	Mean 4.63 ± 2.0
No Polypharmacy	6 (3.6%)
Minor	84 (50.3%)
Major	75 (44.9%)
Excessive	2 (1.2%)
Most Commonly Used Drugs	
Candesartan	81 (48.5%)
Vitamin B Complex	69 (41.3%)
Amlodipin	50 (29.9%)
Folic Acid	43 (25.7%)
Long-Acting Insulin	40 (23.9%)
Atorvastatin	36 (21.5%)
Bisoprolol	28 (16.8%)
Metformin	27 (16.2%)
Gabapentin	27 (16.2%)
Rapid-Acting Insulin	27 (16.2%)
Allopurinol	26 (15.6%)
Omeprazole	20 (11.9%)
Lansoprazole	18 (10.8%)
Acetylsalicylic Acid	16 (9.5%)
Glimepiride	10 (5.9%)
Simvastatin	10 (5.9%)

Out of the 167 patients, a total of 366 drug interactions were identified, 60 of them were classified as Type A or have no known interaction, 306 patients (83.6%) had DDIs. The most common interaction were Type C (45.9%), followed by Type B interaction (31.9%). Type X interaction was found in 0.6% of the patients. (Table 3) Combination of rapid acting and long acting insulin was identified as the most frequent (16.2%) drug pair causing Type C DDIs. (Table 4)

Table 3.
Number of DDIs among the patients

Variable	**f** (%)
DDIs	366 (100%)
Type X	2 (0.6%)
Type D	19 (5.2%)
Type C	168 (45.9%)
Type B	117 (31,9%)
Type A	60 (16.4%)
Lowest Number of DDI	0
Highest Number of DDI	16
Mean ± SD	1.83 ± 2,5

Table 4.
Distribution of DDIs.

Drug Interaction Type X		f (%)
Omeprazole	Clopidogrel	1 (0.6%)
Meloxicam	Diclofenac Sodium	1 (0.6%)
Drug Interaction Type D		n (%)
Simvastatin	Amlodipin	5 (2.9%)
Meloxicam	Acetylsalicylic acid	3 (1.8%)
Acarbose	Gliquidone	2 (1.2%)
Acarbose	Glimepiride	2 (1.2%)
Acarbose	Gliclazide	2 (1.2%)
Gabapentin	Antacid	1 (0.6%)
Sucralfat	Antacid	1 (0.6%)
Ramipril	Candesartan	1 (0.6%)
Sulfat Ferrous	Antacid	1 (0.6%)
Drug Interaction Type C		n (%)
Rapid Acting Insulin	Long Acting Insulin	27 (16.2%)
Bisoprolol	Long Acting Insulin	11 (6.6%)
Bisoprolol	Rapid Acting Insulin	9 (5.4%)
Glimepiride	Metformin	6 (3.6%)
Candesartan	Tamsulosin	6 (3.6%)
Long Acting Insulin	Metformin	6 (3.6%)
Candesartan	Meloxicam	6 (3.6%)
Bisoprolol	Metformin	5 (2.9%)

According to Spearman Correlation Test, factors that significantly associated with DDIs were comorbidities (r = 0.038, p-value = 0.000) and polypharmacy (r = 0.727, p-value = 0.000). We found significant association between comorbidities and polypharmacy (r = 0.463, p-value = 0.000). According to Mann-Whitney U Test, no statistically significant association was found between Sex and other variables. (Table 5).

Table 5.
Bivariate analysis of the variables

r (p-value)	Age	Comorbidities	Polypharmacy	DDIs
Age		0.059 (0.446)	0.141 (0.070)	0.038 (0.623)
Comorbidities			0.463 (0.000)	0.357 (0.000)
Polypharmacy				0.727 (0.000)
Sex	(0.251)	(0.054)	(0.431)	(0.759)

DISCUSSION

Polypharmacy in elderly increased the potential for DDIs and lead to several problems, such as toxicity, adverse drug events, and hospitalisation (Oliveira et al., 2024). Our study showed that most of the respondents are young elderly (47.3%) followed by middle elderly (43.1%) and the least is old elderly (9.6%). This result is similar with the 2023 study on the prevalence of elderly in Indonesia that showed 63.59% were young elderly, 27.76% were middle elderly and 8.65% were old elderly (Badan Pusat Statistik, 2023). This study found no significant difference between age and DDIs (p-value = 0.623), although theoritecally older people are more likely to receive multiple medications due to comorbid conditions and as a result increasing risk of DDIs (Oliveira et al., 2024). Similarly with study done by Endalifer, et al, there was no correlation between age group and number of drugs being used (p-value = 0.924) (Endalifer et al., 2023). However, other study done by Rasool et al. 2020) found significant correlation (p-value = 0.001) between age and frequency of drug interactions. As our study majority population consists of young and middle elderly, differences in age grouping, definition of polypharmacy, these could lead to an insignificant

correlation between age and DDIs.

The most common comorbidities in our respondent were hypertension (73.6%) followed by diabetes mellitus (54.4%), these are in line with the 2019 report from the Indonesian Ministry of Health which showed hypertension and diabetes mellitus among the five most prevalent non-communicable diseases in elderly (Kementerian Kesehatan Republik Indonesia, 2020). A study in India also showed hypertension (73.2%) and diabetes (78%) as the most common comorbidities in geriatric patients. Our study found a significant correlation between number of comorbidities with polypharmacy (p-value = 0.000) and DDIs (p-value = 0.000). This result is in line with study done by Endalifer, et al that found the prevalence of polypharmacy is significantly high with comorbid disease condition (p-value = 0.000) (Endalifer et al., 2023). Faisal, et al also found that patients with excessive polypharmacy had significantly higher comorbidities (p-value <0.01) (Faisal et al., 2024). Rasool et al. 2020) also found significant correlation between comorbidities and the frequency of drug interactions (p-value < 0.002).

In a observational study that examined over 2 billion older Americans' medical visits, polypharmacy was documented in 65.1% of the cases, and patients with major polypharmacy tended to be older than the other categories. In our study, 96.4% patients had taken two or more medications, 46.1% had taken five or more and 1.2% had taken ten or more medications. A study done by Alhumaidi, et al showed that 97% of their patients had taken more than two medications, among whom major polypharmacy was encountered in 79% of the patients (Alhumaidi et al., 2023). Other study in 484 geriatric patients use different classification of polypharmacy showed 21.69% patients were classified polypharmacy (prescription of 6-9 drugs) and 1.24% as hyperpolypharmacy (prescription of ≥10 drugs) (Vegada et al., 2020). The most common drugs used is candesartan (48.5%). This is because the most comorbidity found in our study is hypertension, according to AHA 2025, candesartan and amlodipine are one of the first line to treat hypertension (Jones et al., 2025). Our study found significant correlation between polypharmacy and DDIs (p-value = 0.000), similar with study done by Lozano, et al (p-value < 0.001) and Vegada, et al (p-value < 0.0001) (Lozano-Lozano et al., 2024; Vegada et al., 2020).

Our study demonstrated the most DDIs occurred in our population is type C DDIs (45.9%). This result is similar to a study done by Abdelkawy, et al that found 58% type C DDIs in their population (Abdelkawy et al., 2023). Sari, et al found similar result in their study with 75.5% of their respondents classified as type C DDIs (Sari & Putra, 2024). In the study, the most reported interacting drugs in type C DDIs were rapid and long acting insulin. The concurrent use of the insulin and other blood glucose lowering agents can induce hypoglicemia, mitigation of hypoglicemia risk could be achieved by the selection of appropriate dose, glucose self monitoring and education on hypoglicemia symptoms. (Zhao et al., 2022)

Type X DDIs was found in 0.6% patients. Interaction between Omperazole and Clopidogrel should be avoided as clopidogrel inhibits cytochrome (CYP) P450 isoenzyme 2C19, which attenuates the antiplatelet effect of clopidogrel. Replacement of omeprazole with rabeprazole or pantoprazole is highly recommended (Abed et al., 2020; Alhumaidi et al., 2023). Meloxicam and sodium diclofenac are both categorized as non-selective Cox inhibitors, concurrent use of both of those medicines increase risk of cardiovascular event and gastrointestinal bleeding, it is not recommended to use 2 or more Non-Steroidal Anti-Inflammatory Drugs (NSAID), since concomitant use does not increase the effectiveness and it does increase toxicity (Cheng et al., 2024).

The concurrent use of simvastatin and amlodipine was the most type D DDIs (2.9%) found in our study, amlodipine raises plasma levels of simvastatin and lovastatin through CYP450 enzyme inhibition, this could lead to myotoxicity including rhabdomyolisis with the release of potentially nephrotoxic substances. If the combination therapy of amlodipine and simvastatin is necessary,

simvastatin 24 mg was an optimal dose with amlodipine 10 mg that can minimize the concentration profile (Cheng et al., 2024). Meloxicam and acetylsalicylic acid was found in 1.8% of our respondent. NSAID cause gastrointestinal mucosal damage by inhibition of prostaglandin synthesis, increasing risk of ulceration, bleeding, and perforation, especially when combined with other gastrointestinal irritants. The interaction between NSAID and aspirin is variable and depends on the dose of aspirin, dose of NSAID, and dose timing (Krauss et al., 2020).

Acarbose monotherapy rarely causes hypoglicemia, but if given in combination with other antidiabetic agents such as sulfonylureas or insulins, the risk of hypoglicaemia increased. If hypoglicemia happens, proper adjustments in the dosage of these medicines should be made (Akmal et al., 2024). Our study found no significant correlation between sex and other variables supported by previous studies. However, some studies showed that the prevalence of polypharmacy and DDIs was higher in female due to behavioural factors of female individuals, such as their attitude towards health and willingness to seek care (Faisal et al., 2024). This study has several limitations. Quantitative classification of polypharmacy differs across studies, this might affects the study results. Factors such as drug dosage and the timing of drug administration were not analyzed in detail, as both of them might affect the severity and likelihood of DDIs. In addition, this study was retrospective and did not include direct clinical monitoring of patients. Therefore, the identified DDIs were limited to potential interactions based on medical record data rather than actual clinical events.

CONCLUSION

The present study showed a high prevalence of polypharmacy and potential occurrence of DDIs among geriatric outpatients. Factors such as number of comorbidities and medications were significantly correlated with the occurrence of DDIs. Clinicians need to assess the patients for polypharmacy and DDIs to minimize inappropriate medications. The finding of this study highlights the need for further research and increase awareness to identify and develop preventive measures so that polypharmacy and DDIs can be minimalized.

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